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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/020,450	12/14/2001	Guy Michael Miller	346392000900	1698

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EXAMINER	
SPIVACK, PHYLLIS G	
ART UNIT	**PAPER NUMBER**
1614	12

DATE MAILED: 01/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
10/020,450	Miller et al.
Examiner	**Art Unit**
Phyllis G. Spivack	1614

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 8, 2002*.

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-62* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 8-32, and 51-62* is/are rejected.

7) ☒ Claim(s) *4-7 and 33-50* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5, 10, 11*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Applicants' Amendment filed November 8, 2002, Paper No. 8, is acknowledged. New claims 58-62 are presented. Accordingly, claims 1-62 are now under consideration.

Three Information Disclosure Statements filed September 3 and twice on December 9, 2002, Paper Nos. 6, 10 and 11, respectively, are further acknowledged and have been reviewed.

In the last Office Action claims 1-57 were rejected under 35 U.S.C. 103 as being unpatentable over Wechter, W.J., U.S. Patent No. 6,048,891. It was asserted Wechter teaches the administration of beta, delta and gamma tocopherol or the metabolite, 2,7,8-trimethyl-2-(β-carboxyethyl)-6-hydroxychroman, to treat thromboembolic disease or ischemic conditions and to prevent neuropathological lesions.

Applicants argue Wechter does not describe or suggest the use of non-alpha tocopherols in a method of reducing a symptom of neuronal damage associated with a cerebral ischemic condition.

In view of the amendment to claim 1, such that the claim is now directed to treating a symptom of neuronal damage associated with a cerebral ischemic condition, this rejection of record under 35 U.S.C. 103 is withdrawn.

Claims 1-57 were also rejected in the last Office Action under 35 U.S.C. 103 as being unpatentable over Chabrier et al., WO 98/09653. It was asserted Chabrier teaches the administration of various derivatives of tocopherol, as β-, γ- or δ-tocopherol, to treat neurodegenerative conditions as cerebral infarction.

Applicants argue that although Chabrier teaches a reduction of neuronal damage as a result of cerebral ischemia, the method is only effective when tocopherols are administered in combination with nitrous oxide synthase blocking agents.

Applicants' argument is persuasive and the rejection is withdrawn.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 8-32 and 51-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fryer, M.J., Nutritional Neuroscience.

Fryer teaches the administration of tocopherols for the treatment of both neuronal damage and cerebral ischemic conditions. See column 1 on page 329, where gamma-tocopherol is stated to be far superior to alpha-tocopherol in the detoxification of peroxynitrite, an inflammatory nitrogen oxide that induces lipid peroxidation and is a retrograde messenger generated in post-synaptic neurons. See Table VI on page 345 where examples include both cerebral ischemia and neuronal damage. The claims differ in that neuronal damage and cerebral ischemia are treated by alpha-tocopherol. However, in view of Fryer's teaching, one skilled in the art would have been motivated to administer gamma-tocopherol, or a metabolite thereof, to treat a symptom of neuronal damage associated with a cerebral ischemic condition. Such would have been obvious in

the absence of evidence to the contrary because Fryer discloses, as an effect of the administration of tocopherol, prevention of ischemia-induced neuronal death. The prior art clearly shows gamma-tocopherol to be more potent than alpha-tocopherol in inhibiting platelet aggregation and thrombogenesis. It would have been reasonable to expect one skilled in the art would have selected γ-tocopherol in place of α-tocopherol because γ-tocopherol reduces superoxide anion generation, lipid peroxidation and LDL oxidation, and increases the activity of the enzyme superoxide dismutase, to a much greater extent than α-tocopherol. It is established in the prior art that the harmful effects of free radicals are best counteracted by γ-tocopherol. Thus clear motivation is provided to administer γ-tocopherol in place of α-tocopherol. The selection of both optimal concentrations and modes of administration of the tocopherol are parameters well within the purview of those skilled in the art through no more than routine experimentation.

THIS ACTION IS MADE FINAL. Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however,

will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Phyllis Spivack at telephone number 703-308-4703.

January 17, 2003

Phyllis Spivack

PHYLLIS SPIVACK
PATENT EXAMINER
GROUP 1614